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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/487,792	01/20/00	LAFLEUR	D PF482P1

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HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

HM12/1023

EXAMINER

SEHARASEYON, J

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/487,792

Applicant(s)

Lafleur et al.

Examiner

Sarada C Prasad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-177 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 41-177 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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Detailed Action

1. Receipt of Applicants' arguments and amendments filed in Paper No. 14 (7/6/01) is acknowledged. Currently, claims 41-177 are under consideration.
2. Applicant's arguments filed in Paper No. 7 (8/9/01), have been fully considered but were deemed persuasive in part. The issues remaining and new issues, are stated below.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101/112 first paragraph

- 4a. Claims 41-177 are rejected under 35 USC § 101/112 first paragraph in Paper No.12 (3/7/01).

This rejection of record is being maintained for reasons of record set forth in pages 2-3 of the previous office action (Paper No.12, 3/7/01).

The instant claims are drawn to a polypeptide of SEQ ID No. 2 representing keratinocyte derived interferon (KDI), however, as of yet not shown to have its own identity by way of demonstrated biological effects or functions. The specification shows in Figure 4 an alignment of the KDI polypeptide of the present invention with several other members of the interferon polypeptide family (page 8). While the alignment shows the conserved domains between the various interferons, and the instant KDI polypeptide labeled 'HKAPI15orf' it appears that the identification of the instant SEQ ID No. 2 is based on homology and it is these conserved regions that are the embodiment of the present invention (last two lines of the 4th para, page 8).

Applicants assert that 'based on its structural similarity to IFN-omega and its increased expression in response to stimulated viral infection, KDI is believed to share many of its

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biological activities of IFN-omega and other interferon proteins, including inhibition of tumor proliferation, antiviral activities, NK cell activation and immune system enhancement' (page 3 4th para, Paper No. 14, 7/6/01). However, until some actual and specific significance can be attributed to the polypeptide variants contemplated, the instant invention is incomplete. All of the envisioned polypeptide variants, portions of the polypeptides, fragments are based on the knowledge from the conserved domains of the other interferon molecules, and not specifically attributable to the instant SEQ ID No.2 or its putative variants. In the absence of knowledge of the biological significance of these proteins, there are no immediately obvious patentable uses for these interferon-like proteins. Several of the examples shown are 'prophetic' and do not represent 'real-word' examples, such as contemplating the construction of N-terminal and/or C-terminal deletion mutants: Example 9 states that 'the following general approach may be used to clone N-terminal and/or C-terminal deletion mutants' (page 185, line 1).

Claims 41-177 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

4b. Even if a patentable utility were to be established, the specification would be found to be enabling for only an full length sequence of an isolated polypeptide of SEQ ID No.2 representing an interferon-like protein, encoded by the polynucleotide of SEQ ID No. 1, but not to isolated polypeptides having an amino acid sequence at least 90% or 95% identical to SEQ ID No. 2, or portions of SEQ ID NO. 2 with no specific delimiters, short peptides, or 30 or 50 contiguous amino acids. The specification does not enable any person skilled in the art to which it pertains,

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or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification sets forth a polynucleotide of SEQ ID No. 1 (1170 residue-long) encoding for a possible 207 amino acid residue interferon-like protein of SEQ ID No. 2 (specification, summary of the invention, pages 4-6).

The recitation of 'an isolated polypeptide comprising an amino acid sequence at least 95 or 90% identical to SEQ ID NO. 2' in claims 64, 80 is overly broad. Such claim language can be interpreted to mean that the encoded polypeptides can have up to 5-10% of the amino acids distinct from that encoded by SEQ ID No.1. Considering that SEQ ID No.2 consists of 207 amino acids, up to 6-12 amino acids can be altered at any given time; also considering that the conserved regions are essential to retain interferon-like activity of the KDI polypeptides, and are not available for substitutions, the amino acid changes in the proposed variants would have to be selected from a polypeptide of considerably less than 207 amino acids. The disclosure fails to provide any guidance by way of example for any one of the KDI variants envisioned.

Recitation of 'an isolated protein comprising a polypeptide havingresidues n-207, where n is an integer from 1-58.....' in claims 80 and 94 is extremely broad . This claim language represents several truncated polypeptides with missing segments either at the N-terminus or at the C-terminus of SEQ ID No.2. Without specific guidance, it would be undue experimentation for one of skill in the art to generate several fragments and test their usefulness.

In a similar fashion, recitation of 'an isolated protein comprising a polypeptide havingresidues 49-54, 59-65,204-207 of SEQ ID NO. 2 in claim 117 is extremely broad . This claim language represents several truncated polypeptide segments with missing sequences either

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at the N-terminus or at the C-terminus of SEQ ID No.2. Without guidance in the specification, it would be undue experimentation for one of skill in the art to generate several such fragments and test their usefulness.

Additionally, claim 160 is broad in reciting an isolated protein comprising at least 30 contiguous amino acid residues of SEQ ID No.2. It is not feasible for one of skill in the art which contiguous 30 or 50 amino acids should be selected to prepare the segments of SEQ ID No.2. Without guidance it would require undue experimentation for one of skill in the art to generate such fragments and perform test of their functionality.

The specification lacks sufficient details and guidance to prepare the fragments or contiguous portions of 30 or 50 amino acids of SEQ ID No.2. which would retain functional characteristic of the polypeptide of SEQ ID No.2. It is not feasible for one of skill in the art to generate variants that have features of keratinocyte derived interferon without guidance as to which residues have been altered and found to be dispensable or not dispensable. It is essential to have guidance by way of example or by way of description of methods that have been employed to achieve variants of SEQ ID No.2 with any certainty.

It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino

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acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Given the breadth of claims 53, 64, 80, 94, 106, 117, 136, 148, 160, 169, in light of the predictability of the art that random arbitrary sequence changes do not ensure variants with features of SEQ ID No.2, as determined by the lack of working examples, state of the art suggesting how guidance is needed for a skilled artisan even for single amino acid changes, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112-First paragraph-written description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 53-135, 148-177 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

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convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant written description sets forth a polypeptide of SEQ ID No. 2 representing KDI (pages 8-10). However, the written description is not commensurate with 'an isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence of a polypeptide at least 90 or 95 % identical to an interferon like polypeptide having the amino acid sequence of SEQ ID No.2.

Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the claimed invention. Therefore, the Applicant is not in possession of the invention as claimed, at the time of filing. This is insufficient to support the claims as provided by the Revised Written description Guidelines published in the Federal register, vol 66, No.4, pages 1099-1111, Friday January 2001.

Instant specification provides general principles for making the polypeptide variants of SEQ ID No. 2 encoding the various KDI-like polypeptides variants. However, the disclosure fails to provide detailed description directed to the intended variants of the polypeptide of SEQ ID No.2 exhibiting KDI-like proteins with interferon like function. It is not sufficient to name the claimed variant polypeptides comprising 90% and 95% identity to SEQ ID No. 2, or the variant polypeptides without actually generating any of the said variants, and demonstrating their proper membership in the claimed genus.

Additionally, none of the proposed 'sequence variants' have been shown to be successfully achieved by the claimed nucleotide changes to SEQ ID No. 1 with deletions, replacements or substitutions, and yet have any of the features/properties and biological activity

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characteristic of the intended putative KDI-like protein of SEQ ID No. 2. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species or a structural/functional feature sufficient to describe and enable the genus as broadly claimed. Since the disclosure fails to describe successful generation of any such variants with expected criteria, or describe what are the many permitted amino acid changes while preparing variants of SEQ ID No. 2, it can be reasonably concluded that Applicant is not in possession of the claimed variants at the time of filing.

5b. Claims 53-63, 80-93, 106-116, 148-159, 169-177 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 53, 80, 106, 148, 169 recite the use of cDNA contained in ATCC Deposit No.203500. This deposit is essential to the claimed invention. The reproduction of cDNA that encodes the KDI polypeptide must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public.

If the deposits have been made under the terms of the Budapest treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

- (a) that the ATCC deposit has been deposited under the Budapest treaty; and
- (b) that it will be irrevocably and without restriction or condition be released to the public upon issuance of a patent

would satisfy the deposit requirement made herein. See 37 CFR 1.808.

Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit, or 5 years after the last request for a sample, or for the enforceable life of a patent whichever is longer. See 37 CFR 1.806. If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have not been met.

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Amendment of the specification to disclose the date of deposit and the complete name and the address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the deposits described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a claim of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicants' possession at the time the application was filed. Applicants attention is directed to *In re Lunduk*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claims 54-63, 81-93, 107-116, 149-159, 170-177 are rejected insofar as they depend on claims 53, 80, 106, 148, 169.

Conclusion

6. No claims are allowed.

Gary L. Kunz
GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jagatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached Monday – Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
October 20th, 2001